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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/840,277	04/23/2001	Ulrich Feige	A-688A	3317

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EXAMINER	
WESSENDORF, TERESA D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 08/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/840,277	FEIGE ET AL.	
	Examiner	Art Unit	
	T. D. Wessendorf	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-5,7-9,25 and 26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-5, 7-9, 25 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicants' election of the species poly(Gly-Ala) made on 5/19/2006 is acknowledged.

Status of Claims

Claims 3-5, 7-9, 25 and 26 are pending and under examination.

Claims 1-2, 6 and 10-24 have been cancelled.

Claim 26 is withdrawn with respect to the other non-elected species and examined only to the extent of the elected species, Seq. ID. 136 and poly(Gly-ala).

Withdrawn Rejection

In view of the support for the lambda linker, as pointed out by applicants, the 35 USC 112, first paragraph rejections under new matter and written description has been overcome. Likewise, the 35 USC 112, second paragraph has been overcome.

Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 25, as amended, is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to

particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25, which depends on claim 26, is unclear as to the amino acid sequence being referred to as Seq. ID. Nos. 133-137. It is suggested that applicants positively recite that these amino acid sequences refer to the P variables. (It is also suggested that dependency of the claims be amended. Claim 26 should depend on claim 25, not vice versa.)

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 3-5, 7-9, 25 and 26, as amended, are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitty in view of Mu and Liu et al (6,835,809).

Whitty discloses at page 3, lines 1-27 an isolated polypeptide having the amino acid sequence X--Y--Z, wherein X is a polypeptide having the amino acid sequence, or portion thereof, consisting of the amino acid sequence of interferon beta; Y is an optional linker moiety; and Z is a polypeptide comprising at least a portion of a polypeptide other than interferon beta. Optional moiety Y and required moiety Z may be linked to either the N- or C-terminus of interferon beta (X). Preferably, X is human interferon-beta-1a. Z is at least a

portion of a constant region of an immunoglobulin and can be derived from an immunoglobulin of the IgG class such as IgG1, IgG2, IgG3 and IgG4. See Fig. 3, page 5. Whitty further discloses at paragraph bridging pages 19 and 20, that in the fusion proteins, the interferon-beta-1a polypeptide is fused via its C-terminus to at least a portion of the Fc region of an immunoglobulin. The interferon-beta-1a forms the amino-terminal portion, and the Fc region forms the carboxy terminal portion. Whitty describes at page 20, line 24 up to page 21, line 15, a dimeric fusion molecules as well as monomeric or multimeric molecules comprising fusion proteins. Such multimers may be generated by using those Fc regions, or portions thereof, of Ig molecules which are usually multivalent such as IgM pentamers or IgA dimers. Multimers of interferon-beta-1a fusion proteins may be formed using a protein with an affinity for the Fc region of Ig molecules. The polyvalent forms are useful since they possess multiple interferon beta receptor binding sites. For example, a bivalent soluble interferon-beta-1a may consist of two tandem repeats of amino acids 1 to 166 of SEQ ID NO: 2 (moiety X in the generic formula) separated by a linker region (moiety Y), the repeats bound to at least a portion of an immunoglobulin constant domain (moiety Z). Alternate polyvalent forms may also be constructed, for example, by chemically coupling interferon-

beta-1a/Ig fusions to any clinically acceptable carrier molecule like polyethylene glycol using conventional coupling techniques.

Whitty fails to disclose a fusion protein with laminin of the sequence YIGSR and poly(gly-ala) as the linker. However, Mu discloses that laminin peptide with YIGSR bioconjugated with polystyrene co-maleic acid results in increase of antimetastic effect. See page 75, col. 1 and 2. Mu further discloses that to be therapeutically useful YIGSR peptide requires in vivo stability that allows administration of YIGSR. Mu discloses similar bioconjugation of other extracellular matrix domains, besides YIGSR, such as Interferons. Mu discloses that alone, without any carrier, the small size YISGR undergoes degradation (cf. with the same conclusive finding in the disclosure). Liu discloses at col. 6, line 38 that natural amino acids linker such as polygly in combination with any one of the other 19 natural amino acid render the synthesis of the conjugate(col. 4, line 25 up to col. 5, line 24) accessible to recombinant technologies. See also, col. 10, lines 32-61. Liu further discloses at col. 11, line 7 that a non-peptide linker as polyethylene glycol can also be used as a linker. It would have been obvious to one having ordinary skill in the art at the time the invention was made to replace the interferon in the fusion protein composition of Whitty with a YIGSR-containing laminin,

as taught by Mu. Mu teaches that laminin and interferon belong to the family of extracellular matrix domains (active in adhesion). It would be within the ordinary skill in the art to pick or choose the specific compounds from the family of extracellular matrix domain compounds. Fusion of these peptides to Fc with the extracellular domain compounds, results in increased in vivo stability relative to the non-fused peptide. Such in vivo stability would motivate one having ordinary skill in the art. In vivo stability is an important aspect for therapeutic effect of a compound agent in the treatment of any disease particularly, tumors. To substitute the PEG linker in the composition of Whitty with a natural amino acid linkers as poly(gly-ala) as taught by Liu would have been obvious to one having ordinary skill in the art at the time the invention was made. Liu teaches that these linkers are functionally equivalent linkers but poly(gly-ala) being a natural amino acids renders the synthesis of the conjugate accessible to recombinant technology. This benefit would provide one having ordinary skill in the art to make said linker substitution. Accordingly, the combined teachings of the prior art render the claimed composition prima facie obvious at the time of applicants' invention.

Seq. ID. 136, the elected species, is free of prior art.

Therefore, the examination has been extended to Seq. ID. 7.

No claim is allowed.

Conclusion

Khono discloses Fc fusion with Apo peptide.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D. Wessendorf whose telephone number is (571) 272-0812. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

T.D.-T

T. D. Wessendorf
Primary Examiner
Art Unit 1639

Tdw
July 29, 2006